IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Lynette Robyn Griffiths

Appl. No.

(U.S. National Phase of PCT/GB99/01450; U.S.

Appl. No. (to be assigned))

Int'l Filing Date: May 7, 1999

For: Polymorphism in a Nitric Oxide

Synthase Gene

Art Unit: (To be assigned)

Examiner: (To be assigned)

Atty. Docket: 1581.0720000/RWE/TBB

Information Disclosure Statement

Commissioner for Patents

Box PCT

Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of each of these documents is provided.

The document, AO1, was cited in a search report by a foreign patent office in a counterpart foreign application. Submission of an English language version of the search report that indicates the degree of relevance found by the foreign office is provided in satisfaction of the requirement for a concise explanation of relevance. 1138 OG 37, 38.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

- 2 -Lynette Robyn Griffiths U.S. National Phase of PCT/GB99/01450

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that had been cited or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120. 1138 OG 37, 38 (May 19, 1992).

This Information Disclosure Statement is being filed within three months of the U.S. filing date. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Robert W. Esmond Attorney for Applicant

Registration No. 32,893

Date: Nov. 13,2000

1100 New York Avenue, N.W. Suite 600 Washington, D.C. 20005-3934 (202) 371-2600

529 Rec'd PCT/PTC 13 NOV 2000

	-				ATTY. DOCKET NO. APPLICATION NO. 1581.0720000/RWE/TBB U.S. Nat'l. Phase of PCT/GB99/01450					
		FORM	PTO-1449		APPLICANT Lynette Robyn Griffiths					
	INFORMAT	ION DIS	SCLOSURE STATE	MENT						
					INTERNATIONAL FILING DATE GROUP May 7, 1999 To be assigned					
				U.S.	PATENT DOCUMENTS					
EXAMINER		000	IMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE		
INITIAL	AA1	_	JMENT NUMBER	DATE 04/11/1995	McDermed et al.	514	605	03/22/1993		
			05,872	04/17/1995	Horma et al.	514	303	09/03/1992		
· · · · · · · · · · · · · · · · · · ·	AB1		09,936		···	424	717	04/02/1993		
	AC1	$\overline{}$	76,569	03/05/1996	Morris, Jr. et al.	514	673	01/28/1994		
	AD1	5,5	10,390	04/23/1996	Bergeron, Jr.	. 314	1 8/3	01/28/1994		
	AE			<u> </u>						
	AF AG				***					
	AH	+-								
	AI AI	+								
	AJ		· · · ·							
	AK	1	-							
	,			FOREIG	N PATENT DOCUMENTS					
EXAMINER INITIAL		DOCUMENT NUMBER		DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION		
INTITAL								Y		
	AL1	WO 9	97/33989	09/18/1997	WIPO					
	AM1	wo s	77/38130	10/16/1997	WIPO			Y		
	AN1	wo s	98/02170	01/22/1998	WIPO			Y		
	A01	WO 9	98/08516	05/03/1998	WIPO			X I		
	AP							Y .		
	AF		OTHER (Including Author	Title, Date, Pertinent Pages	. etc.)				
	AR	1	Bellamy, R. and Hill, A.V.S., "A bi-allelic tetranucleotide repeat in the promoter of the huinducible nitric oxide synthase gene," Clin. Genet. 52:192-193, Munksgaard (1997)							
	AS	1	Bloch, K.D. et al "Three Members of the Nitric Oxide Synthase II Gene Family (NOS2A, NOS2B NOS2C) Colocalize to Human Chromosome 17," Genomics 27:526-530, Academic Press, Inc. (1995)							
***	AT	1	Inducible N	itric Oxide Synth	ecular Cloning, Structure, and ase Gene," <i>J. Biol. Chem.</i> 269: iology, Inc. (1994)	i Chromosomal 6765-6772, T	Localization he American S	n of the Human ociety for		
EXAMI NER			<u> </u>	<u> </u>		DATE CONSI	DERED			
EXAMINER: I	nitial if	refer	ence consider	ed, whether or no	t citation is in conformance we de copy of this form with next	ith MPEP 609	. Draw line	through		

09/700270 529 Rec'd PCT/PTC 13 NOV 2000

Page 2 of 6

					ATTY. DOCKET NO. 1581.0720000/RWE/TBB APPLICATION NO. U.S. Nat'l. Phase of PCT/GB99/01450					
		FORM P	TO-1449		APPLICANT Lynette Robyn Griffiths					
<u> 11</u>	IFORMATIC	ON DISC	CLOSURE STATE	<u>MENT</u>	INTERNATIONAL FILING DATE May 7, 1999 GROUP To be assigned					
		· ·		u.s.	PATENT DOCUMENTS	110 De ass	- Igneu			
EXAMINER		DOCU	MENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE		
INITIAL	AA	100001	TENT NUMBER	DATE	INAPIG	OE/100				
	АВ									
	AC									
	AD		<u> </u>							
	AE	ļ	-							
	AF	<u> </u>								
	AG	 	-							
	AH IA	+				 				
	AJ	\vdash	***************************************							
	AK	 								
				FOREI	GN PATENT DOCUMENTS					
EXAMINER INITIAL		DOCU	MENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION		
	AL							Yes No		
	Ť							Yes No		
	AM							Yes		
	AN							No Yes		
	AO	-						No Yes		
	AP	<u> </u>				<u> </u>		No		
			OTHER (Including Author	, Title, Date, Pertinent Pages,	etc.)				
	Deng, A.Y. and Rapp, J.P., "Locus for the Inducible, but Not a Constitutive, Nitric Oxide Synthase Cosegregates with Blood Pressure in the Dahl Salt-sensitive Rat," J. Clin. Invest. 95:2170-2177, The American Society for Clinical Investigation, Inc. (1995)									
	AS	<u>2</u>	Hare, J.M. a Prog. Cardio	Hare, J.M. and Colucci, W.S.,"Role of Nitric Oxide in the Regulation of Myocardial Function," Prog. Cardiovasc. Dis. 38:155-166, W.B. Saunders Co. (1995)						
	АТ	2	Hilbert, P. et al., "Chromosomal mapping of two genetic loci associated with blood-pressure regulation in hereditary hypertensive rats," <i>Nature</i> 353:521-529, Macmillian Publisher Ltd. (1991)							
EXAMINER						DATE CONSIDE	RED			
EXAMINER: Inicitation if no	tial if t in con	refere forman	nce consider ce and not c	ed, whether or no onsidered. Inclu	ot citation is in conformance winde copy of this form with next	th MPEP 609. communicatio	Draw line n to Applica	through ant.		

09/700270 529 Rec'd PCT/PTC 13 NOV 2000 Page 3 of 6

					ATTY. DOCKET NO. 1581.0720000/RWE/TBB APPLICATION NO. U.S. Nat'l. Phase of PCT/GB99/01450					
		FORM I	PTO-1449		APPLICANT Lynette Robyn Griffiths					
<u>I</u>	NFORMAT I	ON DIS	CLOSURE STATE	<u>EMENT</u>	INTERNATIONAL FILING DATE May 7, 1999 GROUP To be assigned					
-				U.S.	PATENT DOCUMENTS					
EXAMINER INITIAL		DOCU	MENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE		
	AA									
	AB	<u> </u>			·		<u> </u> -			
	AC	-				<u> </u>	 			
	AD	-			-		-			
	AE	┿		<u> </u>		_	-			
	AF AG	+-		<u> </u>			†			
	AH	 								
	AI									
	AJ		<u></u>							
	AK									
				FORE I	GN PATENT DOCUMENTS					
EXAMINER INITIAL		DOCU	MENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION		
	AL							Yes No		
	AM							Yes No		
	AN							Yes No		
		1						Yes No		
	AO -	\dagger						Yes No		
	AP		071150 /	Zantoniana Austra	, Title, Date, Pertinent Pages,	oto)	1	NO		
	AR	3	Julier, C. of homology	et al "Genetic	susceptibility for human famili sure linkage on rat chromosome	al essential	hypertension. Genet. 6:2	on in a region 077-2086,		
	AS	3	Lacolley, P. stiffness in (1998)	Lacolley, P. et $al.$, "Nitric oxide synthase gene polymorphisms, blood pressue and aortic stiffness in normotensive and hypertensive subjects," $J.$ Hypertens. 16:31-35, Rapid Science Ltd. (1998)						
	AT	<u>3</u>	Singh, A. e Prehypertens Inc. (1996)	Singh, A. et al., "Inducible Nitric Oxide Synthase in Vascular Smooth Muscle Cells From Prehypertensive Spontaneously Hypertensive Rats," Am. J. Hypertens. 9:867-877, Elsevier Science, Inc. (1996)						
EXAMINER	h					DATE CONSID	ERED			
EXAMINER: Ini	tial if	refere	ence considere	ed, whether or no onsidered. Inclu	ot citation is in conformance wade copy of this form with next	ith MPEP 609.	. Draw line on to Applica	through		

Page 4 of 6 APPLICATION NO. ATTY. DOCKET NO. 1581.0720000/RWE/TBB U.S. Nat'l. Phase of PCT/GB99/01450 FORM PTO-1449 **APPLICANT** Lynette Robyn Griffiths INFORMATION DISCLOSURE STATEMENT INTERNATIONAL FILING DATE **GROUP** May 7, 1999 To be assigned U.S. PATENT DOCUMENTS EXAMINER DOCUMENT NUMBER DATE NAME CLASS SUB-CLASS FILING DATE INITIAL AΑ AB AC AD ΑE AF AG ΑH ΑI LΑ ΑK FOREIGN PATENT DOCUMENTS EXAMINER CLASS SUB-CLASS TRANSLATION DOCUMENT NUMBER DATE COUNTRY INITIAL Yes No ΑL Yes No ΑМ Yes No ΑN Yes No ΑO Yes OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Stepanov, V. et al., "Endothelial nitric oxide synthase gene polymorphism in essential hypertension with or without left ventricular hypertrophy," Eur. J. Human Genetics 6(S1):178, <u>4</u> AR Macmillian Publishers Ltd. (1998) Takahashi, Y. $et\ al$, "Association analysis of TG repeat polymorphism of the neuronal nitric oxide synthase gene with essential hypertension," Clin. Genet. 52:83-85, Munksgaard (1997) AS 4 Tambs, K. et al., "Genetic and Environmental Effects on Blood Pressure in a Norwegian Sample," Genet. Epidemiol. 9:11-26, Wiley-Liss, Inc. (1992) ΑT <u>4</u> DATE CONSIDERED **EXAMINER** EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

09/700270 529 Rec'd PCT/PTC 13 NOV 2000

Page 5 of 6

			-		ATTY. DOCKET NO. 1581.0720000/RWE/TBB APPLICATION NO. U.S. Nat'l. Phase of PCT/GB99/01450				
			PTO-1449		APPLICANT Lynette Robyn Griffiths				
	INFORMAT	ION DIS	SCLOSURE STATE	<u>:MENT</u>	INTERNATIONAL FILING DATE GROUP May 7, 1999 To be assigned				
				U.S.	PATENT DOCUMENTS				
EXAMINER		Poci	IMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE	
INITIAL	- AA	DOCK	JMENT NUMBER	DATE	MAIIC	CEAGG	GOD GENOC	TICING DATE	
-	AB	 -							
	AC								
	AD								
	AE								
	AF								
	AG								
	AH						<u> </u>		
	AI		 	-					
-	LAJ	_					<u></u>		
	AK				· · · · · · · · · · · · · · · · · · ·				
		1		FOREIC	GN PATENT DOCUMENTS	· 	T		
EXAMINER INITIAL		DOCL	JMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION	
	AL							Yes No	
	АМ		· · · · · · · · · · · · · · · · · · ·					Yes No	
		<u> </u>				75		Yes No	
	AN							Yes	
	AO	-						No Yes	
	AP							No.	
			OTHER (Including Author	, Title, Date, Pertinent Pages,	etc.)			
·	AR	<u>5</u>	Synthase and	d Endothelin-1 Ge	tion Study of the 5' Flanking F enes in Familial Primary Open-A , Blackwell Science (1998)	Regions of En ngle Glaucoma	dothelial-Ni ," <i>Clin</i> . & E	itric Oxide Exper	
	AS	5	Uwabo, J. et al., "Association of a Variable Number of Tandem Repeats in the Endothelial Constitutive Nitric Oxide Synthase Gene With Essential Hypertension in Japanese," Am. J. Hypertens. 11:125-128, Elsevier Science Ltd. (1998)						
	AT	<u>5</u>	Xu, W. et al., "Evolution of a homopurine-homopyrimidine pentanucleotide repeat sequence upstream of the human inducible nitric oxide synthase gene," <i>Gene</i> 204:165-170, Elsevier Science B.V. (1997)						
EXAMINER	_1	1	<u> </u>			DATE CONSID	DATE CONSIDERED		
EXAMINER: 1	nitial if	refer	ence consider	ed, whether or no	ot citation is in conformance w	ith MPEP 609.	Draw line	through	

529 Rec'd PCT/PTC 13 NOV 2000

Page 6 of 6

					ATTY. DOCKET NO. 1581.0720000/RWE/TBB APPLICATION NO. U.S. Nat'l. Phase of PCT/GB99/01450					
			то-1449		APPLICANT Lynette Robyn Griffiths					
<u>IN</u>	FORMAT IC	N DIS	CLOSURE STATE	MENT	INTERNATIONAL FILING DATE GROUP May 7, 1999 To be assigned					
				U.S.	PATENT DOCUMENTS					
EXAMINER							01.400	CUD CLASS	FILLING DATE	
INITIAL		DOCUI	MENT NUMBER	DATE	NAME		CLASS	SUB-CLASS	FILING DATE	
	AA AB									
	AC	 	<u>.</u>							
	AD	<u> </u>			· · · · · · · · · · · · · · · · · · ·				······	
	AE	-								
	AF	1			-					
•	AG									
	АН							<u>.</u>		
	ΑI									
	ΑJ					_				
	AK	<u> </u>								
				FOREIC	N PATENT DOCUMENTS					
EXAMINER INITIAL		DOCUI	MENT NUMBER	DATE	COUNTRY		CLASS	SUB-CLASS	TRANSLATION	
	AL								Yes No	
	АМ				· ·				Yes No	
	AN								Yes No	
									Yes No	
	AO								Yes No	
	AP			•	Title Dete Dentin	ant Dagge o	<u> </u>		NO	
			OTHER (Including Author	Title, Date, Pertin	ent Pages, e	tc.)			
	AR	<u>6</u>	Internation	al Search Report	of International App	lication No.	PCT/GB99/0	1450.		
					,					
	-								. <u> </u>	
	AS				•					
	.									
	AT									
EXAMINER	I					D	ATE CONSIDE	RED		
EXAMINER: Init	ial if i	refere forman	nce considere	ed, whether or no onsidered. Inclu	t citation is in cond de copy of this form	formance with	h MPEP 609.	Draw line n to Applica	through	
5. CGC 1011 11 110C										